Remarks

Upon entry of the foregoing amendment, claims 71-95 are pending in this application. Claims 1-70 are canceled without prejudice or disclaimer. Applicants have pursued the subject matter of certain of the cancelled claims herein in the newly added claims and reserve the right to pursue the remaining subject matter in a continuing or divisional application. Claims 71-95 are newly added and are currently under examination. Claims 71 and 81 are the independent claims.

Support for new claims 71-95 is found, for example, in former claims 1-42, 53-57, 59-63, and 65-70 and elsewhere throughout the specification. Applicants have rewritten certain of the former pending claims and then canceled those former claims in order to present the new claims in a succinct format.

Support for new claim 71 is found, for example, as follows:

in original claims 1 and 2;

for the concept of "adjuvant only formulation," on page 19, lines 1-9;

for "adjuvant which is itself antigenic" on page 19, lines 6-9 and lines 24-25; as exemplified in Example 1, Table 1 (CT alone); in Example 5 (CT alone); in Example 3, Table 3 (LT alone); in Example 4 (LT alone); in Example 6, Table 6, (ETA alone); in Example 7, Table 7 (LT alone, CT alone, ETA alone); page 3, line 7; and, elsewhere throughout the specification;

for "modified ADP-ribosylating exotoxins, wherein the modified exotoxin is catalytically inactivated or modified to be less toxic to the organism than the non-modified exotoxin" in original claim 53; page 34, lines 18-23 (inactivating the catalytic activity of the ADP-ribosyl transferase); and, elsewhere throughout the specification.

Support for new claims 72 and 87 is found, for example, in original claim 54; on page 19, lines 10-20; as exemplified in Example 1, Table 1 (CT alone); in Example 5 (CT alone); in Example

3, Table 3 (LT alone); in Example 4 (LT alone); in Example 6, Table 6, (ETA alone); in Example 7, Table 7 (LT alone, CT alone, ETA alone); page 33, lines 28-30 through page 34, line 3; and, elsewhere throughout the specification.

Support for new claim 73 and 88 is found, for example, in original claim 9; on page 9, line 3; and, elsewhere throughout the specification.

Support for new claims 74 and 89 is found, for example, in original claim 10; on page 9, lines 3-5; and, elsewhere throughout the specification.

Support for new claims 75 and 90 is found, for example, in original claim 27; on page 11, lines 23-24; and, elsewhere throughout the specification.

Support for new claims 76 and 91 is found, for example, in original claim 65; on page 17, lines 15-16; and, elsewhere throughout the specification.

Support for new claims 77 and 92 is found, for example, in original claim 66; on page 16, lines 27-29; and, elsewhere throughout the specification.

Support for new claims 78 and 93 is found, for example, in original claim 67; on page 17, lines 1-2; and, elsewhere throughout the specification.

Support for new claims 79 and 94 is found, for example, in original claim 68; on page 41, lines 9-10; and, elsewhere throughout the specification.

Support for new claims 80 and 95 is found, for example, in original claim 69; on page 9, lines 6-9; and, elsewhere throughout the specification.

Support for new claim 82 is found, for example, in original claim 1;

for the concept of co-administration of antigen and adjuvant, in Example 2, Table 2 (CT plus BSA); Example 25, Table 21 (CT plus Hib-PS); and, elsewhere throughout the specification;

for "modified ADP-ribosylating exotoxins, wherein the modified exotoxin is catalytically inactivated or modified to be less toxic to the organism than the non-modified exotoxin" in original claim 53; page 34, lines 18-23 (inactivating the catalytic activity of the ADP-ribosyl transferase); and, elsewhere throughout the specification.

Support for new claims 82 and 83 is found, for example, in original claims 25, 28 and 29-32; page 17, lines 24-25; and elsewhere throughout the specification.

Support for new claim 84 is found, for example, on page 29, lines 3-12 and lines 25-end through page 30, line 11; in original claim 39; and, elsewhere throughout the specification.

Support for new claim 85 is found, for example, in Example 44 (page 125), Table 43, page 126, showing an antibody response to killed rabies virus.

Support for new claim 86 is found, for example, in original claim 56; on page 19, lines 20; and, elsewhere throughout the specification.

No new matter is believed to have been added by this amendment. In view of the amendments and following remarks, reconsideration of the rejections and withdrawal thereof is respectfully requested.

The Office Action dated June 3, 2003 has been carefully reviewed and the foregoing amendments are made in response thereto.

Rejection of claims 1-42, 53-57, 59-63 and 65-69 under 35 U.S.C. § 112, first paragraph

Claims 1-42, 53-57, 59-63 and 65-69 remain rejected under 35 USC § 112, first paragraph, because the specification while being enabled for "a method for transcutaneous immunization comprising applying a formulation that does not include a heterologous adjuvant to intact skin, said formulation consisting of cholera toxin (CT), LT or ETA to hydrated skin does not reasonably provide enablement for:

b) a method for TCI comprising activating at least one antigen presenting cell underlying the site of formulation application (ie claim 5);

c) a method for TCI comprising an APC wherein the APC is a Langerhans cell (ie claim 4);

d) a method for TCI comprising applying an antigen in whole cell form (ie claim 40);

e) a method for TCI comprising applying an antigen comprising a viral particle or virion (ie claim 39);

f) a method for TCI comprising applying diptheria toxin (DT) (ie claim 54 in part);

g) a method for TCI wherein the induced immune response recognizes a lipopolysaccharide (ie claim 55);

h) a method for TCI wherein the induced response recognizes influenza virus hemagglutinin (HA)….. (ie claim 56); and,

i) a method for TCI wherein underlying endosomes or lysosomes are lysed (ie claim 57).

Applicants respectfully traverse the rejection.

Without acquiescing to the position of the Office, claims 1-42, 53-57, 59-63 and 65-69 have been canceled without prejudice or disclaimer of the subject matter therein. Applicants reserve the right to pursue claims directed to the canceled subject matter not further prosecuted herein in the new claims in a continuing or divisional application. The rejection is not believed to apply to new claims 71-95 for reasons set forth below.

Contrary to the Examiner's arguments, support for the subject matter of the canceled claims is

described in the specification. Former claim 39 and new claims 83-85 are directed to a pathogen, wherein the pathogen is a virus, wherein the virus is an inactivated virus and specifically to the heat killed rabies virus. Support for former claim 39, now included in the subject matter of new claims 83-85 is found, for example, in Example 44 (page 125), Table 43, page 126, showing an antibody response to killed rabies virus. Support for the subject matter of former claim 54, now new claims 72 and 87 comprising applying diptheria toxin (DT), is found in Example 22, Table 18; and, elsewhere in the specification. Support for former claim 56, now new claim 86 is found, for example, in Table 42 (showing HA results); in Table 21 (showing Hib-PS results); in Table 31 (showing CS6 results); on page 19, line 16 (influenza nucleoprotein (NP)); and, elsewhere throughout the specification.

In view of the cancellation of claims 1-42, 53-57, 59-63 and 65-69, the addition of new claims and the arguments above, the rejection is believed to be moot. Reconsideration and withdrawal of the rejection is respectfully requested.

New rejection of claims 1-42, 53-57, 59-63 and 65-69 under 35 U.S.C. § 112, first paragraph (genetically modified ADP-ribosylating exotoxins)

Claims 1-42, 53-57, 59-63 and 65-69 stand rejected under 35 USC § 112, first paragraph, because the specification while being enabled for applying a formulation which does not include a heterologous adjuvant to intact skin, said formulation consisting of CT, LT or ETA, to hydrated skin, does not reasonably provide enablement for a method of TCI comprising applying a formulation of consisting of genetically modified ADP-ribosylating exotoxins. The rejection is respectfully traversed.

Claims 1-42, 53-57, 59-63 and 65-69 have been canceled. Pertinent to the rejection are new claims 71 and 81. New claims 71 and 81 do not recite the phrase "genetically modified "and the new claim language ("modified ADP-ribosylating exotoxins, wherein the modified exotoxin is catalytically inactivated or modified to be less toxic to the organism than the non-modified

exotoxin") is believed to moot the rejection. Support for the concept, and claim language, is found, for example, on page 34, lines 21-24, describing modified ADP-ribosyl transferases. The modified ADP-ribosyl transferase is obtained by inactivating the catalytic activity of the ADP-ribosyl transferase. The toxins retain the binding capabilities, but lack the toxicity, of the natural toxins. In addition, the specification discloses other toxins whose modification occurs by activation using trypsin cleavage or disruption of disulphide bonds. Activation of PT, for example, via trypsin cleavage is disclosed on page 36, lines 13-22. Activation of LT is described on page 35, lines 18-20. Example 35 demonstrates the use of other modified ADP ribosylating exotoxins. In Example 35, modified LT toxins were used: LTK63, an enzymatically inactive LT derivative and LTR72, an LT derivative which retained only 0.6% of the unmodified LT's enzymatic activity. Both LTK63 and LTR72 are demonstrated in Example 35 to show adjuvant activity when co-administered with DT. LTK63 is further discussed in Example 28 which also discloses non-toxic mutants of CT-CTK63. Specification page 33, beginning at line 6 through page 36, line 22, discusses the structure function relationship of the ADP-ribosylating exotoxins. Applicants assert the specification provides sufficient guidance to one of ordinary skill to make modified ADP-ribosylating exotoxins wherein the modified form is less toxic than the unmodified form and that no undue experimentation would be required. Reconsideration and withdrawal of the rejection is respectfully requested.

Rejection of claims 1-42, 53-57, 59-63 and 65-69 under 35 U.S.C. § 112, first paragraph (written description regarding genetically modified ADP-ribosylating exotoxins)

Claims 1-42, 53-57, 59-63 and 65-69 remain rejected under 35 USC § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor, at the time the application was filed, has possession of the claimed invention. The rejection is respectfully traversed.

The instant rejection is related to the previous rejection under 35 USC § 112, above, asserting lack of enablement. The arguments presented above are pertinent and are incorporated herein by

reference. The claim language of new claims 71 and 81 is believed to moot the rejection. Reconsideration and withdrawal of the rejection is respectfully requested.

Provision Rejection under the judicially created Doctrine of Obviousness Type Double Patenting

Claims 1-42, 53-57, 59-63 and 65-69 stand provisionally rejected under the judicially created Doctrine of Obviousness Type Double Patenting as being unpatentable over claims 3-35, 50-77 and 79-111 of copending application no. 09/266,803. Applicants respectfully traverse the provisional rejection.

Claims 1-42, 53-57, 59-63 and 65-69 have been canceled and new claims 71-95 have been added. Reconsideration and withdrawal of the rejection is respectfully requested.

Conclusion

The foregoing amendments and remarks are being made to place the application in condition for allowance. Applicants respectfully request reconsideration and the timely allowance of the pending claims. A favorable action is awaited. Should the Examiner find that an interview would be helpful to further prosecution of this application, the Examiner is invited to telephone the undersigned at his convenience.

Except for issue fees payable under 37 C.F.R. § 1.18, the Commissioner is hereby authorized by this paper to charge any additional fees during the entire pendency of this application including fees due under 37 C.F.R. § 1.16 and § 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account 50-0310.

This paragraph is intended to be a **Constructive Petition for Extension of Time** in accordance with 37 C.F.R. § 1.136(a)(3).

Respectfully submitted,
Morgan, Lewis & Bockius LLP

Erich E. Veitenheimer, III, Ph.D.
Registration No. 40,420

Date: **December 3, 2003**
Morgan, Lewis & Bockius LLP
Customer No. **009629**
1111 Pennsylvania Ave., N.W.
Washington, D.C. 20004
202.739.3000